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1-18. (canceled)

19. A method of producing aflibercept, comprising:

(a) producing a clarified harvest of a cells cultured in a chemically defined medium (CDM);

(b) binding aflibercept from said clarified harvest to a Protein A resin, wherein said aflibercept includes variants that have at least one oxidized amino acid residue selected from the group consisting of tryptophan, histidine, phenylalanine, tyrosine and a combination thereof;

(c) eluting said aflibercept of step (b) forming an affinity eluate, wherein said eluate comprises oxidized species of aflibercept;

(d) subjecting said eluted aflibercept to anion exchange (AEX) chromatography column; and

(e) collecting a flowthrough fraction, wherein the percent of oxidized species of aflibercept in said affinity eluate is greater than the percent of oxidized species of aflibercept in said flowthrough fraction when the concentrations of protein in said eluate and flowthrough fraction are normalized, and

wherein said oxidized species of aflibercept is measured by subjecting said affinity eluate and said flowthrough fractions to digestion, followed by their analysis using reverse-phase ultra-performance chromatography (UPLC), detection at wavelengths of 280 nm, 320 nm and 350 nm and mass spectrometry analysis using a first mobile phase of 0.1% v/v formic acid in water and a second mobile phase of 0.1% v/v formic acid in acetonitrile.

20. The method of claim **19**, wherein the percent of oxidized species of aflibercept in said flowthrough fraction is reduced by at least about 10% compared to the percent of oxidized species of aflibercept in said affinity eluate.

21. (canceled)

22. The method of claim **19**, wherein said oxidized amino acid residue is selected from an amino acid residue on a polypeptide having an amino acid sequence as set forth in the group consisting of: SEQ ID NO.: 17, SEQ ID NO.: 18, SEQ ID NO.: 19, SEQ ID NO.: 20, SEQ ID NO.: 21, SEQ ID NO.: 22, SEQ ID NO.: 23, and SEQ ID NO.: 67.

23. (canceled)

24. A method of producing aflibercept, comprising:

(a) producing a clarified harvest of a cells cultured in a chemically defined medium (CDM), wherein said clarified harvest comprises one or more aflibercept variants, wherein said variants have at least one oxidized amino acid residue selected from the group consisting of tryptophan, histidine, phenylalanine, tyrosine and a combination thereof;

(b) collecting a protein sample from said clarified harvest, wherein said protein sample comprises aflibercept and at least one aflibercept variant, and wherein said protein sample has a b* value of more than 0.5 when the concentration of said protein sample is normalized to 10.0 g/L;

(c) binding aflibercept from said clarified harvest to a first capture chromatography;

(d) eluting said aflibercept of step (c) forming an eluate, wherein said eluate has a first color; and

(e) subjecting said elaute to an anion exchange chromatography (AEX) column; and

(f) collecting a flowthrough fraction, wherein said flowthrough fraction has a second color, and wherein said first color is more intense yellow-brown color than said second color when said eluate and said flowthrough fraction protein concentrations are normalized.

25. The method of claim **24**, wherein said first capture chromatography comprises Protein A resin.